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REMARKS

The Office action of November 24, 2006, has been carefully considered.

The specification has been amended to provide a reference to the PCT application.

Claims 16-17, 21-29 and 31 have been rejected under 35 USC 102(b) as being anticipated by de Haan et al.

This rejection is based upon the contention that the present claims read on conventional liposomes as might be used by de Haan et al, citing in this context U.S. Patent No. 4,522,803 which states at column 2, line 27-34, that "liposomes are...multilamellar vesicles (onion-like structures characterized by concentric membrane bilayers each separated from the next by a layer of water)."

A similar issue was dealt with in co-pending application Serial No. 09/536,153, owned by the Assignee of the present application. In that application, in order to establish the distinction between the claimed vesicles (such as are disclosed in the Roux et al reference) and the liposomes of De Haan et al, a declaration was submitted from Anne Bernheim-Groswasser presenting therein a photomicrographic study of vesicles according to the invention, in comparison with multilamellar vesicles according to the prior art, and especially multilamellar vesicles of U.S. Patent No. 4,975,282, assigned to the Liposome Company, Inc. It can be seen clearly that in the vesicles of the invention, the bilayers are concentric and extend from the very center of the vesicle to its periphery; this is not the case for the classical multilamellar vesicles in which the bilayers cannot be considered to be concentric and regularly stacked from the center to the periphery.

While the claims of the present application do not

specifically recite that the vesicles comprise a regular stack of bilayers from the center of the vesicles to the periphery (as did the claims of Serial No. 09/536,153), it is noted that the present claims recite that the vesicles have a "liquid crystal structure" which means that the stack is regular and without a substantial core. In the vesicles of the prior art (Fig. 1 of the declaration), there is a very substantial core, and the bilayers are quite irregular.

As Applicants have now clearly established that the vesicles of the invention are not the same in structure as the multilamellar vesicles of the prior art, withdrawal of this rejection is requested.

Claims 16-17 and 21-35 have been rejected under 35 USC 103(a) over De Haan et al, by itself or in combination with Roux et al, with De Haan et al cited to show the mucosal administration of liposomal antigens, and Roux et al cited to show the vesicles of the invention. Alternatively, Claims 16-19, 21-33 and 35-65 have been rejected under 35 USC 103(a) over Wassef et al in combination with De Haan et al by itself, or in further combination with Doerschuk and Roux et al.

To the extent that these combinations of references create a presumption of *prima facie* obviousness, Applicants now submit herewith a Declaration of inventor Rene Laversanne to show unexpected results.

At the interview on August 29, 2005, inventor Laversanne pointed out that the De Haan et al reference required liposomes formed from negatively charged lipids, whereas the claimed invention did not have any such requirement. The comparative testing done took into account this teaching of De Haan et al, and in particular, testing was carried out at two different volumes of administration, and using uncharged and negatively charged liposomes/vesicles.

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A control was also included.

Results are given in Table 4 of the declaration and in Figures 1 and 2. From the table and the figures, it can be seen that utilizing the liposomes of the prior art, a negative charge is indeed required, with the antibody response resulting from uncharged liposomes not substantially greater than the control. The antibody response utilizing the liposomes of the prior art is indeed much greater when negatively charged liposomes are utilized. However, when the vesicles of the invention are used, the overall response is much greater than when liposomes of the prior art are used, and the difference between negatively charged and uncharged vesicles is relatively small. When a larger quantity of sample is administered, the liposomes of the prior art do elicit a much greater response, but generally less than the response which is elicited utilizing the vesicles of the invention. The inventor believes that this "volume effect" resulting in amplification of the immune response is at least partially due to antigen reaching the lungs. For safety reasons, this is to be avoided in actual immunization schemes for humans.

Accordingly, Applicants have now established by comparative testing the unexpected superiority of mucosal immunization carried out utilizing the vesicles of the claimed invention, as compared with immunization with prior art vesicles as used by De Haan et al.

Wassef et al teach the use of prior art multilamellar vesicles as carriers for vaccines, so one would not expect the superiority obtained utilizing the vesicles of the invention.

Withdrawal of these rejections is requested.

In view of the foregoing amendments and remarks, Applicants submit that the present application is now in

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condition for allowance. An early allowance of the application with amended claims is earnestly solicited.

Respectfully submitted,

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